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08/259,321	06/10/94	REZAIE A	OMRF106CIP

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EXAMINER	
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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 35

Application Number: 08/259,321
Filing Date: June 10, 1994
Appellant(s): Rezaie and Esmon

Patrea L. Pabst
For Appellant

EXAMINER'S ANSWER

This is in response to appellant's brief on appeal filed January 4, 2000.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is incorrect. The amendment after final rejection filed on January 4, 2000 has been entered.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

Appellant's brief includes a statement that claims 1-3, 5, 7,8, 14, 15, 17-21 do not stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

The following is a listing of the prior art of record relied upon in the rejection of claims under appeal.

5,553,101	Queen	6/25/96
5,202,253	Esmon	4/13/93

5,147,638 Esmon 4/13/92

D'Angelo, Journal Clinical Investigation, 77:416-425, 1986

Stearns, New England Journal of Medicine, 262(2(:826-832, 1988

Morrison, Science 229:1201-7, 1985

WO 90/07861, Queen, July 26, 1990

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 1-3, 5, 7-8, 1415 and 17-21 are rejected under 35 U.S.C. § 103 as being unpatentable over any of U.S. Patent No. 5,202,253 (the '253 patent), U.S. Patent No. 5,147,638 (the '638 patent), D'Angelo or Stearns in view of view of Morrison, Queen (WO 90/07861) or Queen (U.S. Patent 5,530, 101, 6/25/96, filed 12/19/90).

The teachings and motivations provided by the cited references have been covered at length in previous office actions. Briefly, each of U.S. Patent No. 5,202,253, U.S. Patent No. 5,147,638, D'Angelo and Stearns teach monoclonal antibody HPC4 and the hybridoma cell line that secretes the HPC-4 antibody. These references do not teach the humanization of said antibody or its synthesis in bacterial or insect cells. However, Morrison and the two Queen references teach the complete methodology for the cloning and sequencing cDNA from the hybridoma cell line that secretes a given murine monoclonal antibody the nucleotide sequences that encode the immunoglobulin heavy and light chains (For example, see Example 5 of the Queen '101 patent) and complete methodologies for the construction of a humanized antibody using the hypervariable sequences obtained from these nucleotide sequences.

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the basic methodology taught by Queen in order to clone the genes encoding the HPC-4 monoclonal antibody from the hybridoma cell line ATCC No. HB 9892 taught by U.S. Patent No. 5,202,253 or U.S. Patent No. 5,147,638, D'Angelo and Stearns. In doing so one of ordinary skill in the art would have obtained antibodies having the structural characteristics of those claimed. One of ordinary skill in the art would have been motivated to

produce recombinant antibodies having the variable region of HPC-4 in order to obtain the advantages discussed by Morrison, for example, on page 1207. One would have been motivated to produce chimeric antibodies or humanized antibodies comprising human antibody sequences in view of the art-recognized advantages of reduced immunogenicity in human hosts obtained by replacing rodent antibody sequences with human sequences as discussed by Morrison and Queen.

Claims 1-3, 5, 7-8, 14-15 and 17-21 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 5,202,253 in view of Morrison or Queen, for reasons of record in previous office actions.

(11) Response to Argument

First, the applicant argues that the claimed antibody can not be obtained absent the cloning of the gene encoding the variable regions of the HPC-4 antibody and it is well established under US law that it is not obvious to obtain a specific nucleotide sequence based only on the protein.

This is not found persuasive. The nucleotide sequence is obvious in view of teachings of the hybridoma cell line that secretes the HPC-4 antibody protein, and not merely the HPC-4 protein. Combining this hybridoma cell line with the methodologies for cloning and sequencing immunoglobulin variable region sequences taught in the Queen and Morrison references, the nucleotide sequence of the HPC-4 heavy and light chain variable regions (and thus, the amino acid sequences of the heavy and light chain) is obvious to one of skill in the art. The level of skill in the art of the cloning the genes encoding antibodies was very high at the time of filing of the instant application, the applicant admits as much. The combined teachings make the nucleotide sequence obvious and make the claimed antibodies and methods obvious.

Second, the applicant argues that even if cloning were obvious, one of skill in the art could not have predicted that it was merely the amino acid sequence forming the variable region of the HPC-4 murine antibody that was responsible for the unique protein-calcium binding specificity of the antibody. These statements are mere assertions, unsupported by fact. While the HPC4 antibody may demonstrate a unique binding specificity, imparted by the unique amino acid sequence of its hypervariable regions, there is absolutely no evidence of record to indicate that the overall structure of the HPC4 antibody differs in any fashion from that of all antibodies in general and that such a variation from well known immunoglobulin structure plays a role in the unique binding specificity of the HPC4 antibody. All antibodies, whether murine or human, share a high degree of structural homology, in the constant regions and the framework regions of the variable regions. Unique binding specificities are imparted to the antibody by the amino acid sequences of the hypervariable regions. One of skill in the art would reasonably expect the hypervariable regions of the HPC-4 antibody, when transplanted to a human antibody framework, would maintain the HPC-4 binding specificity.

The applicant argues that for the same reasons as argued against the rejection of the claims

under 35 U.S.C. § 103, the rejection of the claims under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 5,202,253 in view of Morrison or Queen is inappropriate. For the same reasons presented above, this is not found persuasive.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

NAJ
July 31, 2000

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